

# PATENT COOPERATION TREATY

**PATENT DEPARTMENT  
RECEIVED**

From the INTERNATIONAL SEARCHING AUTHORITY

# PCT

To:

SCHERING CORPORATION  
Patent Department K-6-1 1990  
2000 Galloping Hill Road  
Kenilworth, NJ 07033-0530  
UNITED STATES OF AMERICA

JUN 26 2002

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*HE 6/27/02*

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NOTIFICATION OF TRANSMITTAL OF  
THE INTERNATIONAL SEARCH REPORT  
OR THE DECLARATION

(PCT Rule 44.1)

Date of mailing:  
(day/month/year)

07/06/2002

Applicant's or agent's file reference

IN01159K

**FOR FURTHER ACTION**

See paragraphs 1 and 4 below

International application No.

PCT/US 01/ 22678

International filing date  
(day/month/year)

19/07/2001

Applicant

SCHERING CORPORATION

1. ☒ The applicant is hereby notified that the International Search Report has been established and is transmitted herewith.

**Filing of amendments and statement under Article 19:**

The applicant is entitled, if he so wishes, to amend the claims of the International Application (see Rule 46):

**When?** The time limit for filing such amendments is normally 2 months from the date of transmittal of the International Search Report; however, for more details, see the notes on the accompanying sheet.

**Where?** Directly to the International Bureau of WIPO  
34, chemin des Colombettes  
1211 Geneva 20, Switzerland  
Fascimile No.: (41-22) 740.14.35

**For more detailed instructions,** see the notes on the accompanying sheet.

2. ☐ The applicant is hereby notified that no International Search Report will be established and that the declaration under Article 17(2)(a) to that effect is transmitted herewith.

3. ☐ **With regard to the protest** against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

☐ the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.

☐ no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. **Further action(s):** The applicant is reminded of the following:

Shortly after **18 months** from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90bis.1 and 90bis.3, respectively, before the completion of the technical preparations for international publication.

Within **19 months** from the priority date, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later).

Within **20 months** from the priority date, the applicant must perform the prescribed acts for entry into the national phase before all designated Offices which have not been elected in the demand or in a later election within 19 months from the priority date or could not be elected because they are not bound by Chapter II.

Name and mailing address of the International Searching Authority



European Patent Office, P.B. 5818 Patentlaan 2  
NL-2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

Authorized officer

Joannes Vergoosen

## NOTES TO FORM PCT/ISA/220

These Notes are intended to give the basic instructions concerning the filing of amendments under article 19. The Notes are based on the requirements of the Patent Cooperation Treaty, the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the PCT Applicant's Guide, a publication of WIPO.

In these Notes, "Article", "Rule", and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions respectively.

### INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international publication. Furthermore, it should be emphasized that provisional protection is available in some States only.

#### What parts of the international application may be amended?

Under Article 19, only the claims may be amended.

During the international phase, the claims may also be amended (or further amended) under Article 34 before the International Preliminary Examining Authority. The description and drawings may only be amended under Article 34 before the International Examining Authority.

Upon entry into the national phase, all parts of the international application may be amended under Article 28 or, where applicable, Article 41.

#### When?

Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

#### Where not to file the amendments?

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been/is filed, see below.

#### How?

Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Administrative Instructions, Section 205(b)).

The amendments must be made in the language in which the international application is to be published.

#### What documents must/may accompany the amendments?

##### Letter (Section 205(b)):

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confused with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

The letter must be in English or French, at the choice of the applicant. However, if the language of the international application is English, the letter must be in English; if the language of the international application is French, the letter must be in French.

## NOTES TO FORM PCT/ISA/220 (continued)

The letter must indicate the differences between the claims as filed and the claims as amended. It must, in particular, indicate, in connection with each claim appearing in the international application (it being understood that identical indications concerning several claims may be grouped), whether

- (i) the claim is unchanged;
- (ii) the claim is cancelled;
- (iii) the claim is new;
- (iv) the claim replaces one or more claims as filed;
- (v) the claim is the result of the division of a claim as filed.

The following examples illustrate the manner in which amendments must be explained in the accompanying letter:

1. [Where originally there were 48 claims and after amendment of some claims there are 51]:  
"Claims 1 to 29, 31, 32, 34, 35, 37 to 48 replaced by amended claims bearing the same numbers; claims 30, 33 and 36 unchanged; new claims 49 to 51 added."
2. [Where originally there were 15 claims and after amendment of all claims there are 11]:  
"Claims 1 to 15 replaced by amended claims 1 to 11."
3. [Where originally there were 14 claims and the amendments consist in cancelling some claims and in adding new claims]:  
"Claims 1 to 6 and 14 unchanged; claims 7 to 13 cancelled; new claims 15, 16 and 17 added." or  
"Claims 7 to 13 cancelled; new claims 15, 16 and 17 added; all other claims unchanged."
4. [Where various kinds of amendments are made]:  
"Claims 1-10 unchanged; claims 11 to 13, 18 and 19 cancelled; claims 14, 15 and 16 replaced by amended claim 14; claim 17 subdivided into amended claims 15, 16 and 17; new claims 20 and 21 added."

### "Statement under article 19(1)" (Rule 46.4)

The amendments may be accompanied by a statement explaining the amendments and indicating any impact that such amendments might have on the description and the drawings (which cannot be amended under Article 19(1)).

The statement will be published with the international application and the amended claims.

It must be in the language in which the international application is to be published.

It must be brief, not exceeding 500 words if in English or if translated into English.

It should not be confused with and does not replace the letter indicating the differences between the claims as filed and as amended. It must be filed on a separate sheet and must be identified as such by a heading, preferably by using the words "Statement under Article 19(1)."

It may not contain any disparaging comments on the international search report or the relevance of citations contained in that report. Reference to citations, relevant to a given claim, contained in the international search report may be made only in connection with an amendment of that claim.

### Consequence if a demand for international preliminary examination has already been filed

If, at the time of filing any amendments under Article 19, a demand for international preliminary examination has already been submitted, the applicant must preferably, at the same time of filing the amendments with the International Bureau, also file a copy of such amendments with the International Preliminary Examining Authority (see Rule 62.2(a), first sentence).

### Consequence with regard to translation of the international application for entry into the national phase

The applicant's attention is drawn to the fact that, where upon entry into the national phase, a translation of the claims as amended under Article 19 may have to be furnished to the designated/elected Offices, instead of, or in addition to, the translation of the claims as filed.

For further details on the requirements of each designated/elected Office, see Volume II of the PCT Applicant's Guide.

## PCT

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference <b>IN01159K</b>	<b>FOR FURTHER ACTION</b> see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. <b>PCT/US 01/ 22678</b>	International filing date (day/month/year) <b>19/07/2001</b>	(Earliest) Priority Date (day/month/year) <b>21/07/2000</b>
Applicant  <b>SCHERING CORPORATION</b>		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 3 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

## 1. Basis of the report

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☒ **Certain claims were found unsearchable** (See Box I).

3. ☐ **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,

☐ the text is approved as submitted by the applicant.

☒ the text has been established by this Authority to read as follows:

**PEPTIDES AS NS3-SERIN PROTEASE INHIBITORS OF HEPATITIS C VIRUS**

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

☐ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

☒ None of the figures.

# INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 01/22678

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07K5/062 C07K5/065 A61K38/05 A61P31/14

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07K A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, BIOSIS, CHEM ABS Data, WPI Data

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
E	WO 01 74768 A (VERTEX PHARMA ;COURT JOHN (US); MALLEY ETHAN O (US); PERNI ROBERT) 11 October 2001 (2001-10-11) claims; examples ---	1-38
P,X	WO 01 40262 A (DU PONT PHARM CO) 7 June 2001 (2001-06-07) claims; examples ---	1-38
P,X	WO 00 52032 A (DAINIPPON) 8 September 2000 (2000-09-08) & EP 1 157 998 A 28 November 2001 (2001-11-28) claims; examples --- -/--	1-38

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

\* Special categories of cited documents:

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

- \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- \*&\* document member of the same patent family

Date of the actual completion of the international search

28 May 2002

Date of mailing of the international search report

07/06/2002

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

Authorized officer

Fuhr, C

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 01/22678

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	HAN WEI ET AL: "alpha-Ketoamides, alpha-ketoesters and alpha-diketones as HCV NS3 protease inhibitors." BIOORGANIC & MEDICINAL CHEMISTRY LETTERS, vol. 10, no. 8, 17 April 2000 (2000-04-17), pages 711-713, XP002199468 ISSN: 0960-894X the whole document ---	1-38
X	WO 99 07734 A (BAILEY MURRAY DOUGLAS ;BOEHRINGER INGELHEIM CA LTD (CA); HALMOS TE) 18 February 1999 (1999-02-18) compounds 103, 109, 112, 115, 116, 225, 227, 229 claims; tables 1,2 ---	1-38
X	LLINAS-BRUNET MONTSE ET AL: "Studies on the c-terminal of hexapeptide inhibitors of the hepatitis C virus serine protease." BIOORGANIC & MEDICINAL CHEMISTRY LETTERS, vol. 8, no. 19, 6 October 1998 (1998-10-06), pages 2719-2724, XP002199470 ISSN: 0960-894X compounds 14 and 18 ---	1-38
X	WO 98 17679 A (DEININGER DAVID D ;MURCKO MARK A (US); VERTEX PHARMA (US); FARMER) 30 April 1998 (1998-04-30) compound 80 claims -----	1-38

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 01/22678

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 0174768	A	11-10-2001	AU 5116501 A WO 0174768 A2	15-10-2001 11-10-2001
WO 0140262	A	07-06-2001	AU 2055301 A WO 0140262 A1	12-06-2001 07-06-2001
WO 0052032	A	08-09-2000	JP 2000256396 A AU 2690200 A CN 1349542 T EP 1157998 A1 WO 0052032 A1 NZ 513594 A TR 200102540 T2	19-09-2000 21-09-2000 15-05-2002 28-11-2001 08-09-2000 28-09-2001 21-01-2002
WO 9907734	A	18-02-1999	AU 8846698 A WO 9907734 A2 EP 1012180 A2 HU 0100100 A2 JP 2001512744 T US 6143715 A	01-03-1999 18-02-1999 28-06-2000 28-11-2001 28-08-2001 07-11-2000
WO 9817679	A	30-04-1998	AP 1019 A AT 212037 T AU 719984 B2 AU 5147798 A BG 103392 A BR 9712544 A CN 1238780 A CZ 9901340 A3 DE 69709671 D1 DK 932617 T3 EE 9900161 A EP 1136498 A1 EP 0932617 A1 HU 0000152 A2 JP 2001502694 T NO 991832 A NZ 335276 A PL 332872 A1 SK 51099 A3 TR 9901602 T2 WO 9817679 A1 US 6265380 B1 US 2002032175 A1 ZA 9709327 A	16-10-2001 15-02-2002 18-05-2000 15-05-1998 31-01-2000 19-10-1999 15-12-1999 11-08-1999 21-02-2002 22-04-2002 15-12-1999 26-09-2001 04-08-1999 28-07-2000 27-02-2001 17-06-1999 29-09-2000 25-10-1999 10-04-2000 21-10-1999 30-04-1998 24-07-2001 14-03-2002 11-05-1998

## FURTHER INFORMATION CONTINUED FROM PCT/SA/ 210

## Continuation of Box I.2

Present claims 1-38 relate to an extremely large number of possible compounds, compositions and methods. In fact, the claims contain so many options and possible permutations that a lack of clarity (and/or conciseness) within the meaning of Article 6 PCT arises to such an extent as to render a meaningful search of the claims impossible. Consequently, the search has been carried out for those parts of the application which do appear to be clear (and/or concise), namely those compounds recited in the examples and in claim 39 and closely related homologous compounds and the compositions and methods relating to them.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US 01/22678

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:  
  
Although claims 35 and 36 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☒ Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:  
  
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

### Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.



<p>(51) 国際特許分類 C07K 5/103, 5/083, C07D 239/54, 233/34, A61K 38/55, A61P 43/00, 11/00</p>	<p>A1</p>	<p>(11) 国際公開番号 WO00/52032</p> <p>(43) 国際公開日 2000年9月8日 (08.09.00)</p>
<p>(21) 国際出願番号 PCT/JP00/01022</p> <p>(22) 国際出願日 2000年2月23日 (23.02.00)</p> <p>(30) 優先権データ 特願平11/56052 1999年3月3日 (03.03.99)</p> <p>(71) 出願人 (米国を除くすべての指定国について) 大日本製薬株式会社 (DAINIPPON PHARMACEUTICAL CO., LTD.) [JP/JP] 〒541-8524 大阪府大阪市中央区道修町2丁目6番8号 Osaka, (JP)</p> <p>(72) 発明者 ; および (75) 発明者 / 出願人 (米国についてのみ) 佐藤文憲 (SATO, Fuminori) [JP/JP] 〒651-2242 兵庫県神戸市西区井吹台東町3丁目1番21号 Hyogo, (JP) 井上泰尚 (INOUE, Yasunao) [JP/JP] 〒532-0002 大阪府大阪市淀川区東三国3丁目11番 24-602号 Osaka, (JP) 面谷智喜 (OMODANI, Tomoki) [JP/JP] 〒666-0011 兵庫県川西市出在家町18番12-206号 Hyogo, (JP) 白武亮太郎 (SHIRATAKE, Ryotaro) [JP/JP] 〒572-0002 大阪府寝屋川市成田東が丘3丁目17番 Osaka, (JP)</p>		<p>本多清二 (HONDA, Seiji) [JP/JP] 〒657-0811 兵庫県神戸市灘区長峰台2丁目6番8号 Hyogo, (JP) 小宮雅信 (KOMIYA, Masanobu) [JP/JP] 〒617-0828 京都府長岡京市馬場井料田3番地14号 Kyoto, (JP) 武村 忠 (TAKEMURA, Tadashi) [JP/JP] 〒562-0044 大阪府箕面市半町4丁目12番地11-503号 Osaka, (JP)</p> <p>(74) 代理人 青山 稔, 外 (AOYAMA, Tamotsu et al.) 〒540-0001 大阪府大阪市中央区城見1丁目3番7号 IMPビル 青山特許事務所 Osaka, (JP)</p> <p>(81) 指定国 AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, 欧州特許 (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI特許 (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG), ARIPO特許 (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), ユーラシア特許 (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM)</p> <p>添付公開書類 国際調査報告書</p>
<p>(54) Title: HETEROCYCLIC COMPOUNDS, INTERMEDIATES THEREOF AND ELASTASE INHIBITORS</p> <p>(54) 発明の名称 複素環式化合物およびその中間体ならびにエラスターゼ阻害剤</p> <div data-bbox="381 1270 1153 1375"> <p style="text-align: right;">(I-a)</p> </div> <p>(57) Abstract Heterocyclic compounds represented by general formula (I-a), its esters or salts thereof; and human neutrophilic elastase inhibitors, etc. containing the same as the active ingredient wherein A and B are the same or different and each represents lower alkylene optionally substituted by oxo; D represents a monocyclic or dicyclic heterocyclic group optionally substituted by oxo; R<sup>1</sup> and R<sup>2</sup> are the same or different and each represents lower alkyl; R<sup>3</sup> and R<sup>4</sup> are different from each other and each represents hydrogen or hydroxy, or R<sup>3</sup> and R<sup>4</sup> form together oxo; and R<sup>5</sup> represents 2-benzoxasolyl, trifluoromethyl, benzylaminocarbonyl, etc.</p>		